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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,476	09/27/2001	Michael Mendez	40977	5080

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EXAMINER
AKHAVAN, RAMIN

ART UNIT	PAPER NUMBER
1636	

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DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

3/21/05 RA

Office Action Summary	Application No.	Applicant(s)	
	09/762,476	MENDEZ ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of an amendment, filed 01/06/2005, as well as a response filed 09/30/2004. Claims 7 and 32 are currently pending and under consideration in this action. All objections/rejections not repeated herein are hereby withdrawn. Where applicable, a response to Applicant's arguments will be included in the body of any objections/rejections maintained. As new grounds of rejection are set forth, this action is NONFINAL.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the new rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

1. **Claims 7 and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Elledge et al. (US 56,828,093; see whole document; hereinafter the '093 patent).**

This is a new ground of rejection. The claims are drawn to a vector system for cloning large nucleic acids and delivery of the cloned nucleic acid to a target cell, where the composition comprises a first arm with a first selectable marker, a first cyclization element and a first segment homologous to the 5' terminus of a target polynucleotide and a second arm with a second selectable marker, second cyclization element and second segment homologous to the 3' terminus of the target polynucleotide, wherein the target nucleic acid is a virus, particularly DNA virus, more particularly a DNA virus such as adenovirus. The limitation of "first" and "second arm" is interpreted as broadly as reasonable, as such the arms can be contained on different regions of a circular or linear construct. Furthermore, the limitation "large nucleic acids" is interpreted as broadly as reasonable to mean any sized nucleic acid predicated on the fact that the term is not delimited to any particular fragment size. In addition, the limitation "cyclization" is interpreted as broadly as reasonable in light of the definition provided in the specification (p. 18, last ¶), as any sequence capable of promoting circularization of the vector arms.

The '093 patent teaches recombinant vectors that contain two cyclization elements (i.e., lox sites), two selection markers (e.g., Ampicillin and Kanamycin resistance and a gene of interest that would necessarily contain some portions that are homologous to 5' and 3' regions of said gene. (e.g., Figures, 1, 12, 14, 20 and 24; col. 14, ll. 7-27, 45-65; col. 15, ll. 7-20; col. 15, last ¶ bridging to col. 16; col. 17, ll. 20-65, bridging to col. 18; col. 20, ll. 25-45). In addition, the gene of interest can be DNA from an adeno-associated virus. (col. 21, l. 27). Furthermore, a suitable host for the vector is *E. coli.* (col. 15, l. 66). In sum, the '093 patent anticipates the rejected claims.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. **Claims 7 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US 5,348,886; see whole document; hereinafter '886 patent), further in view of Elledge et al. (US 6,828,093).**

The '886 patent was the basis of a rejection made previously and is applied herein in conjunction with the '093 patent. A response to Applicant's argument is set forth immediately following the body of this rejection, insofar as Applicant's argument is applicable to what the '886 patent teaches. The claims are interpreted consonant with the interpretation provided in the rejection above. (Supra, § 102(e) Rejection).

The '886 patent teaches a composition comprising viral DNA, a first region (i.e. arm) containing a first genetic marker (i.e. selectable marker; e.g. β-gluc), a preferential target site for insertion of a tansposon (i.e. cyclization element; e.g. attTn7-phoS), a second genetic marker (e.g. Amp) and a second specific insertion site (i.e. cyclization element; e.g. attTn7-glmS). (e.g. col. 3, ll. 20-35; col. 5, ll. 35-40; Fig. 4). The '886 patent teaches, that the composition can comprise viral DNA. (e.g. col. 3, ll. 20-24; Fig. 4). As such parts of this viral DNA could intrinsically be construed as part of the first and second arm.

Furthermore, these particular regions, being part of a contiguous fragment of viral DNA, would have homologous regions to 5' and 3' ends of a corresponding piece of viral DNA. In addition, *E. coli* is taught as containing the composition. (e.g., col. 16, ll. 65-68, bridging to col. 17, ll. 1-5). In sum, the '886 patent anticipates the rejected claims.

The '886 patent does not teach the particular DNA or RNA viruses. However, the '886 patent explicitly teaches that heterologous DNA comprised in the vector can be from any source. (e.g., col. 6, l. 5).

As stated above, the '093 patent anticipates the rejected claims, whereby a vector having arms that each contain a selectable markers, a cyclization elements and regions of a gene of interest that would contain portions that are homologous to 5' and 3' regions of said gene of interest. (See supra, § 102(e) Rejection, describing what the '093 patent teaches). In addition, the '093 patent explicitly teaches that the nucleic acid of interest (i.e., target nucleic acid for expression) can be from adeno-associated virus (AAV). (e.g., col. 21, line 27).

Therefore, it would have been obvious to use viral DNA from various species as taught by the '093 patent and as is suggested by the '886 patent.

One of ordinary skill in the art would be motivated to substitute the viral DNA as suggested by the '886 patent with the AAV nucleic acids as suggested by the '093 patent, so as to expand the range of nucleic acid species manipulated using the recombinant vectors taught by both references. Given the knowledge and skill at the time of the invention, with regard to the species of viruses known in the art, there would have been a reasonable expectation of success in substituting the heterologous DNA system with viral DNA from AAV, as the manipulation would the routine procedure of replacing one nucleic acid molecule with another.

Response to Arguments

Applicant's arguments are in response to the '886 patent under a 35 U.S.C. § 102(b) rejection that is not maintained. However, the arguments presented are applicable to the '886 patent and what it teaches under the instant 35 U.S.C. § 103(a) rejection, thus a response to Applicant's arguments is set forth. Applicant's arguments are summarized as grounded in three assertions. First, Applicant asserts that the '886 patent does not teach delivery of large nucleic acids. (Response, filed 09/30/2004, p. 4, middle ¶). Second, Applicant asserts that the '886 patent does not teach or suggest cloning steps utilizing a virus such as AAV. Finally, Applicant asserts that the *attTn7* transposition elements are preferential target sites, thus Applicant implies that such elements are not capable of promoting circularization. (Response, p. 5, top).

With respect to delivery of large nucleic acids, a vector that is used to mobilize a target nucleic acid does "deliver" large nucleic acids. The limitations "large" and "delivery" are not limiting to the extent that actual boundaries are set for the size of the nucleic acid molecule.

In addition, delivery is interpreted as broadly as reasonable in light of the specification, which does not delimit the term "delivery" to any appreciable extent. Therefore, any composition that comprises a recombinant cloning vector with the elements of two regions that each comprise a selectable marker, cyclization element and nucleic acid molecule of interest that has portions of 5' and 3' homology to like-nucleic acid molecules, would read on the claims.

With respect to the target nucleic acid molecule comprising AAV polynucleotide, the '886 patent explicitly states that target nucleic acids can be viral, as discussed above. Notably, the '886 patent is utilized in an obviousness type rejection, thus the reference, as currently applied, does not necessarily have to teach every element. Practically speaking this particular ground of rejection is moot. However, insofar as Applicant's argument could be extended to the obviousness type rejection, the motivation to provide viral nucleic acids as target molecules is provided in the '886 patent. (e.g., col. 6, l. 5).

Finally, Applicant asserts that the transposon element attTn7 is not a cyclization element. While Applicant is correct in asserting that said element serve as preferential target sites, Applicant is incorrect in implying that such elements are incapable of circularization. Indeed, there is evidence in the art to the contrary that provides the intrinsic capability of attTn7 elements to circularize. Specifically, two AttTn7 transposon elements are capable of forming a lariat (i.e., loop or circle), which is stabilized by a transposase nucleoprotein complex. (e.g., Whittle et al. Modern Microbial Genetics, Second Ed. Wiley-Liss, Inc. 2002; pp. 400-405, especially p. 402, Fig. 7). In other words, attTn7 elements *are* capable of circularizaton. Therefore, Applicant's final ground of traversal must also fail.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached between 8:30-5:00, Monday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD, can be reached on 571-272-0781. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully submitted,
Ray Akhavan/AU 1636

GERRY LEFFERS
PRIMARY EXAMINER